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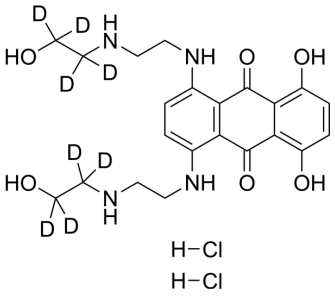
Mitoxantrone-d_8 dihydrochloride

Cat. No.:	HY-13502AS
Molecular Formula:	$C_{22}H_{22}D_8Cl_2N_4O_6$
Molecular Weight:	525.45
Target:	Endogenous Metabolite; PKC; Apoptosis; Topoisomerase; Orthopoxvirus; Isotope-Labeled Compounds
Pathway:	Metabolic Enzyme/Protease; Epigenetics; TGF-beta/Smad; Apoptosis; Cell Cycle/DNA Damage; Anti-infection; Others
Storage:	Please store the product under the recommended conditions in the Certificate of Analysis.



BIOLOGICAL ACTIVITY

Description

Mitoxantrone-d_8 dihydrochloride is deuterated labeled Mitoxantrone dihydrochloride (HY-13502A). Mitoxantrone dihydrochloride is a potent topoisomerase II inhibitor. Mitoxantrone dihydrochloride also inhibits protein kinase C (PKC) activity with an IC_{50} of 8.5 μM. Mitoxantrone dihydrochloride induces apoptosis of B-CLL (B-chronic lymphocytic leukaemia) cells. Mitoxantrone dihydrochloride shows antitumor activity[1][2][3][4]. Mitoxantrone dihydrochloride also has anti-orthopoxvirus activity with EC_{50}s of 0.25 μM and and 0.8 μM for cowpox and monkeypox, respectively[5].

In Vitro

Stable heavy isotopes of hydrogen, carbon, and other elements have been incorporated into drug molecules, largely as tracers for quantitation during the drug development process. Deuteration has gained attention because of its potential to affect the pharmacokinetic and metabolic profiles of drugs[1].

Mitoxantrone dihydrochloride inhibits PKC in a competitive manner with respect to histone H1, and its K_i value is 6.3 μM and in a non-competitive manner with respect to phosphatidylserine and ATP[2].

?Mitoxantrone dihydrochloride (0.5 μg/mL, 48 h) induces a decrease in B-CLL cells. Mitoxantrone dihydrochloride induces DNA fragmentation and the proteolytic cleavage of poly(ADP-ribose) polymerase (PARP), demonstrating that the cytotoxic effect of Mitoxantrone dihydrochloride is due to induction of apoptosis[3].

?Mitoxantrone dihydrochloride shows cytotoxicity to human breast carcinoma cell lines MDA-MB-231 and MCF-7 with IC_{50} values of 18 and 196 nM, respectively[4].

MCE has not independently confirmed the accuracy of these methods. They are for reference only.

In Vivo

Mitoxantrone dihydrochloride (IP, 0-3.2 mg/kg/day) produces a statistically significant number of 60-day survivors at 1.6 mg/kg in mice with IP implanted L1210 leukemia[5].

?Mitoxantrone dihydrochloride (IV, 0-3.2 mg/kg/day) shows effective antitumor activities and produces a 60% ILS (increase in lifespan) at 3.2 mg/kg in SC implanted Lewis lung carcinoma[5].

MCE has not independently confirmed the accuracy of these methods. They are for reference only.

REFERENCES

[1]. Takeuchi N, et al. Inhibitory effect of mitoxantrone on activity of protein kinase C and growth of HL60 cells. J Biochem. 1992 Dec;112(6):762-7.

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[3]. Bellosillo B, et al. Mitoxantrone, a topoisomerase II inhibitor, induces apoptosis of B-chronic lymphocytic leukaemia cells. Br J Haematol. 1998 Jan;100(1):142-6.

[4]. Venza I, et al. Class II-specific histone deacetylase inhibitors MC1568 and MC1575 suppress IL-8 expression in human melanoma cells. Pigment Cell Melanoma Res. 2013

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[5]. Fujimoto S, et al. Antitumor activity of mitoxantrone against murine experimental tumors: comparative analysis against various antitumor antibiotics. Cancer Chemother Pharmacol. 1982;8(2):157-62.

[6]. Russak EM, et al. Impact of Deuterium Substitution on the Pharmacokinetics of Pharmaceuticals. Ann Pharmacother. 2019 Feb;53(2):211-216.

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